P55 *ACHROMOBACTER XYLOSOXIDANS*: FOLLOW-UP OF 20 PATIENTS WITH CHRONIC INFECTION

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Background: *A. xylosoxidans* (Ax) is capable of persistent infection of the respiratory tract of Cystic Fibrosis patients although its contribution to pulmonary decline in this population is not clear.
Aim: To evaluate pathogenic role of Ax studying lung function and nutritional status in CF patients with chronic Ax infection.
Methods: Data (FEV1, FVC, BMI, sputum and number of IV therapy) of 20 CF patients in follow-up at our centre were studied retrospectively at the time of establishment of infection (T0), one year before (T-1) and one year after (T+1) and were then compared. Statistical analysis was performed by Student's T test. Mean age of the 20 (13 females) patients was 14.5 (range 6.2–23.3) at T0.
Results: Lung function showed a slight decrease in the year before the acquisition of Ax both in FVC (91.2±20.4 vs 86.1±12.6%/predicted $p=0.22$) and FEV1 (84.4±20.5 vs 79.1±16.3 %/predicted $p=0.09$), without reaching statistical significance. Respiratory data showed no deterioration in the year after infection: FVC (88.4±18.1 vs 86.1±12.6%/predicted $p=0.47$) and FEV1 (82.9±23.2 vs 79.1±16.3 %/predicted $p=0.26$). However, the number of respiratory exacerbations was much higher in the year after colonisation as demonstrated by the i.v. treatment mean days per patient (12.1±15.5 vs 3.1±6.5, $p=0.03$).
Nutritional status remained unchanged during the study period as demonstrated by BMI of T-1 vs T0 (18.1±2.9 vs 18.1±3.1 $p=0.77$) and T0 vs T+1 (18.1±3.1 vs 18.7±2.9 $p=0.07$).
Conclusion: The pathogenic role of chronic infection by Ax seems to be relevant in terms of therapeutic burden for patients in the short-term. A key factor would be monitoring the evolution of the patients chronically infected by Ax.

P56 OXIDATIVE STATUS CHANGE IN CYSTIC FIBROSIS (CF) AND ORAL ADDITION WITH WHEY PROTEIN ISOLATE WITH HIGH CONTENT OF CYSTEINE: PRELIMINARY OBSERVATIONS

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Oxidative status has a role in the progressive lung damage in CF. Glutathione is an important defence from pro-antioxidant agents and it is reduced in CF. Cysteine is the amino acid that gives to glutathione antioxidant status. The objective of this study is to reduce the oxidative status in CF with oral addition of whey protein isolate with high content of cysteine (PROther). We recruit CF patients older than 6 years, with a FEV1<70%, with a BMI <21 kg/m2 in adults and with a weight <25° centile in children. Oxidative status is estimated on a blood sample with d-ROMs test and BAP test that can measure oxidative stress and antioxidant status respectively. The study has started in May 2007 and will last for 12 months. Patients will be checked every three months. We have planed the enrolment of 50 patients at least. During the follow-up at every examination we will control oxidative status, clinical conditions (nutritional status, growth, lung function), compliance to the administration of PROther, alimentary intake and Quality of life. We recruited 32 patients still now. All cases show a pathological condition of oxidative status. Oxidative stress is increased in all patients and in 52% of cases is very serious. Antioxidant status is normal in 46% of cases and 14% show a high deficiency. Four patients deserted the study for a bad compliance to the administration of PROther not related to the product. In 6 patients we have done the first control after three months from the recruitment. All these cases show an improved oxidative status. Oxidative stress has become normal in one patient. Antioxidant status has become normal in 4 cases. All 6 patients report subjective clinical improvement. On the base of the clinical parameters, respiratory and nutritional conditions are stable in 4 cases and improved in 2. The quality of life test is better in all patients. Collected data confirm a high level of oxidative status in CF patients. Oral addition of whey protein isolate with high content of cysteine seems efficacious to improve the oxidative status. Oxidative status improvement could correlate to a clinical improvement. These observations coming from preliminary data must be confirmed. We think useful to continue the valuation of the efficacy of oral addition of PROther and we consider antioxidant therapy potentially important in CF.

P57 CYTOKINE PROFILES IN DIFFERENT MATRIXES (SERUM, SPUTUM AND EXHALATE) OF CYSTIC FIBROSIS PATIENTS

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The hallmarks of cystic fibrosis (CF) lung disease are bacterial infections by opportunistic pathogens and chronic inflammation, characterized by polymorphonucleate neutrophils predominance, progressing to obstructive lung disease and bronchiectasis.
High levels of sputum tumor necrosis factor (TNF)-α and interleukin (IL)-8 and serum IL-6 have been found in CF patients. The aim of this study was to analyze the major cytokines such as IL-1α, IL-1β, IL-2, IL-4, IL-6, IL-10, interferon (IFN)-γ, the chemokines IL-8, monocyte chemoattractant protein-1 (MCP-1) and the growth factors epidermal growth factor (EGF) and vascular endothelial growth factor (VEGF) before and after antibiotic therapy in serum, sputum and exhalate in order to clarify the process involved in the CF inflammation and to evaluate which is the best matrix which can define this process.
We considered 10 CF patients (median age 19.5± 4, 6 M, 4 F) who were admitted at the CF Center of the University of Milan for i.v. antibiotic therapy during acute respiratory exacerbation. Before and after treatment all patients underwent routine laboratory determinations, sputum culture and standard spirometry. Serum, sputum and exhalate interleukins, chemokines and growth factors were analyzed simultaneously by means of the Evidence® biochip array (Randox) on semiautomated instrument. Results at admission and the percentage of significant changes after six months are reported in the table. After treatment, chemokines and growth factors decreased in a different manner for the considered matrix, only VEGF seemed to be always significantly decreased. No significant change was found for IFN-γ, IL-6 and IL-4.

	pg/ml	IL-2	IL-4	IL-6	IL-8	IL-10	VEGF	IFN-γ	TNF-α	IL-1α	IL-1β	MCP	EGF
Serum	Mean	5.8	4.1	34.7	378	1.5	187	3.41	8.06	0.68	2.28	367	135
	SD	4.6	3.5	69.0	935	1.4	128	3.59	5.83	0.74	2.82	286	107
	change (%)	−26					−41		−34			−28	−56
Sputum	Mean	6.9	12.2	10.5	21852	6.2	2297	1.66	153	102	1344	66	493
	SD	11.0	6.1	12.4	15540	10.9	1412	5.71	239	123	1103	72	548
	change (%)						−78			−41	−56	73	−10
Exhalate	Mean	2.1	4.6	0.2	0.4	0.6	12.2	3.43	1.79	0.43	1.24	2.47	0.60
	SD	4.0	4.9	0.3	0.2	1.1	32.2	9.74	3.93	0.22	2.11	3.94	0.25
	change (%)				−17	−52	−75			−12	−59		

In conclusion, antibiotic therapy in CF patients could be monitored by cytokine profiles in sputum and serum, while exalate levels are too low to be useful. VEGF, a growth factor involved in tissue remodeling, needs further studies.

P58* CYSTIC FIBROSIS RELATED DIABETES IS ANTICIPATED BY REDUCED INSULIN SECRETION DURING OGTT

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Diabetes in Cystic Fibrosis (CFRD) is increasingly common with advancing age because of a combination of insulin resistance and insulin secretory defects. Many patients are normoglycemic or even hypoglycemic after overnight fast, and there are repeated changes of glucose tolerance status from normal to diabetes and vice-versa, for many years and for unclear reasons. These features render difficult the prediction of CFRD development.
This study aimed to detect predictive factors of CFRD development in patients routinely undergoing yearly Oral Glucose Tolerance Test (OGTT) evaluations.
Starting from 2002, all patients followed at the CF Center in Milan aged >10 years and without established CFRD undergo OGTT yearly. Among those who received their first OGTT between 2002 and 2004, 14 had developed definitive diabetes by April 2007. Each of them was matched with patients of same sex and age, who underwent an OGTT in the same month and year but did not develop CFRD ($n=20$). Logistic regression, controlled for age, sex and follow-up time, was used to identify CFRD predictors among factors including glucose, insulin and c-peptide concentrations and area under the curve (AUC) during OGTT, insulin sensitivity indexes (HOMA and QUICKI).
In the group that developed CFRD, baseline glucose concentration was increased (92±6 vs 72±3 mg/dl, mean±SEM, $p=0.034$) whereas insulin and c-peptide concentrations were similar (5.4±0.61 vs 7.8±1.4 μU/ml, and 1.4±0.1 vs 1.4±0.2 ng/ml). Glucose ($p=0.010$) and insulin AUCs ($p=0.030$) were the most important